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| EXAMINER |
|---|
| THOMAS, TIMOTHY P |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1614 | |

| NOTIFICATION DATE | DELIVERY MODE |
|---|---|
| 02/27/2008 | ELECTRONIC |

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/804,023 | LEWIS, MICHAEL D. | |
| | Examiner | Art Unit | |
| | TIMOTHY P. THOMAS | 1614 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *08 January 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-21* is/are pending in the application.

4a) Of the above claim(s) *1-18* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *19-21* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *3/19/2004*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

## DETAILED ACTION

### *Election/Restrictions*

1. Applicant's election with traverse of Group I, claims 19-21, in the reply filed on 1/8/2008 is acknowledged. The traversal is on the ground(s) that the criteria (a)-(e) in the Restriction Requirement do not set out specifics with respect to the instant fact pattern with any particularity; i.e., the undue burden is not apparent on its face. This is not found persuasive because the prior art reference applicable to the elected invention is not applicable to the non-elected invention. Specifically, the rejection which is outlined below anticipates or obviates invention I, a composition that contains a combination of donepezil and chlorpromazine; invention II is drawn to a method of treating a prion disease with only donepezil, none of the prion disease species of the claims is mentioned in the prior art reference used. Therefore, the prior art used in the rejection of claims 19-20 would not be applicable to invention II.

The requirement is still deemed proper and is therefore made FINAL.

2. Applicant's election with traverse of specie (ii), a combination of the two active compounds, donepezil (formula (IV))and chloromazine (it is assumed applicant meant chlorpromazine, which is recited in claim 19) in the reply filed on 1/8/2008 is acknowledged. The traversal is on the ground(s) that the particular specifics with respect to the instant fact pattern are not laid out. This is not found persuasive because a search for one, two or three active compounds in different combinations requires different search quearies for each specific combination, and the prior art that anticipates some of these combinations will not anticipate all possible combinations of the species.

The requirement is still deemed proper and is therefore made FINAL.

3. Claims 1-18 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 1/8/2008.

***Claim Rejections - 35 USC § 112***

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 19-21 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Each of these claims recites a combination of active compounds which can be interpreted in more than one way because of multiple “and”s and “or”s connecting the species, each of these scenarios requires a different minimum number of active compounds, as follows: 1) for claims 19 or 21, the “at least one” therapeutically effective compound can be interpreted as being a minimum of one compound, selected from (a) mepacrine, (b) a pharmaceutically acceptable salt of mepacrine, (c) chlorpromazine, (d) a pharmaceutically acceptable salt of chlorpromazine, (e) donepezil (formula (IV), (f) a pharmaceutically acceptable salt of donepezil, or (g) a stereoisomer of (e) or (f); 2) for claims 19-21, a minimum of two compounds are required, where the first is “at least one compound” selected from (a)-(d) and the second is selected from (e)-(g); 3) for claims 19-21, a minimum of 3 compounds: the first is “at least one compound” selected from

(a)-(b), the second is (c) or (d), the third is selected from (e)-(g). These alternate interpretations do not make clear which combinations are required as minimum components of the claims. Because of the two species elected (the combination of (c) and (e)), it is assumed that either scenario 1) or 2) is meant by applicant.

***Claim Rejections - 35 USC § 102 / 103***

6. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

8. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

9. Claims 19-20 are rejected under 35 U.S.C. 102(e) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Woolf, et al. (US 2003/0073608; filed 2001 Apr 10).

Woolf teaches a process for treating Alzheimer's disease, by sequential administration of 1) an antagonist of a neurotransmitter receptor that indirectly inhibits phosphorolation of microtubule-associated protein-2 (MAP-2 antagonist), followed by 2) an anticholinesterase agent (abstract); combinations of the two active ingredients into a single implant are taught (an optional embodiment of paragraph 0078); the process is used to reduce progressive neuronal degeneration due to Alzheimer's disease (paragraph 0009); suitable candidates of 1) MAP-2 antagonists include muscarinic antagonists (paragraph 0016) and dopamine antagonists (paragraph 0018), the antipsychotic compound specie chlorpromazine is named as a preferred specie (both a dopamine and muscarinic antagonist; paragraph 0023); and 2) aricept (donepezil) is named as a commercially available acetylcholinesterase inhibitor (paragraph 0059). Implants are taught that may be used to administer the cholinesterase inhibitors of the invention (e.g., donepezil) with a biodegradable slow release carrier, these implants may also be used for delivering one or more antagonists (e.g., chlorpromazine) (implying the combination of a MAP-2 antagonist and a acetylcholinesterase in a single pharmaceutical composition; paragraph 0078); time release tablets and capsules are also taught (claims 11-12); an embodiment of dosing at least once a day is taught (paragraph 0038). The combination within paragraph, in consideration with the very few named MAP-2 agonists and acetylcholinesterase compound species implies the

composition of the instant claims. On the other hand, it might be argued that Woolf does not clearly teach the combination of the compound species donepezil and chlorpromazine, together in a single composition. Considering such a point of view, it would have been obvious to combine the two elected active ingredients into a single composition (e.g., an implant, or a time release tablet or capsule), since Woolf names only a few compounds as MAP-2 antagonists or anticholinesterase agents, and since both of the elected compounds are named, they would be obvious choices in such a formulation. The motivation to select chlorpromazine and donepezil for a single composition would be the art-recognized suitability of each elected compound for the purpose taught by Woolf; the motivation to form a single composition (containing single dosages of both chlorpromazine and donepezil) would have been the ease of administration of a combination therapy, which would simplify administration for an aging patient with Alzheimer's disease still living at home, after an initial MAP-2 antagonist dose, as preferred by the method of Woolf (paragraph 0045), was administered by a health care professional. Administration of a combined composition would greatly simplify some of the embodiments of the method taught by Woolf, which become quite complex and would require a complex apparatus and likely hospitalization (which is not likely to be popular with patients or their families; see Figure 2). Enhanced patient compliance with the therapy would be the result of home administration of the obviated combination tablet or capsule.

10. Claim 21 is rejected under 35 U.S.C. 103(a) as being unpatentable over Woolf, et al. (US 2003/0073608; filed 2001 Apr 10) as applied to claims 19-20 above, and further in view of McHugh, et al. (US 2002/0106406 A1; filed 2000).

Woolf does not teach a kit. McHugh teaches polymer composites containing a boactive agent for use as an implant, which allows the release profile by control of the composition of the implant (title, abstract); example drugs include chlorpromazine (paragraph 0044); and a kit containing the active mixture, with unit dosage of active agent and a container (claims 42, 43). It would have been obvious to one of ordinary skill in the art at the time of the invention to use a container that holds separate unit dosages of the composition anticipated or obviated by Woolf (i.e., delayed release unit dosages of both chlorpromazine and donepezil in a container). The motivation to prepare a kit would have been to inform a patient of appropriate information about the drugs by including instructions, and/or to use separate compartment regions of the container (say a 7-compartment or 30-compartment region container), which would permit daily tracking of whether a dosage had been administered, simplifying administration for an Alzheimer's patient.

***Conclusion***

11. No claim is allowed.

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to TIMOTHY P. THOMAS whose telephone number is (571)272-8994. The examiner can normally be reached on Monday-Thursday 6:30 a.m. - 5:00 p.m..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel can be reached on (571) 272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Timothy P Thomas/
Examiner, Art Unit 1614

/Ardin Marschel/
Supervisory Patent Examiner, Art Unit 1614